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October 8, 2004  
Date

  
Shelley P.M. Fussey

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:  
Brewer, Merajver and Coucouvanis

Serial No.: 10/625,839

Filed: July 23, 2003

For: Tetrapropylammonium Tetrathiomolybdate  
and Related Compounds for Anti-  
Angiogenic Therapies

Group Art Unit: 1614

Examiner: Unknown

Atty. Dkt. No.: 4100.003200

**INFORMATION DISCLOSURE STATEMENT**

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Sir:

In compliance with the duty of disclosure under 37 C.F.R. § 1.56, it is respectfully requested that this Information Disclosure Statement be entered and the documents listed on attached Form PTO-1449 be considered by the Examiner and made of record in the present case. Copies of the listed documents required by 37 C.F.R. § 1.98(a)(2) are enclosed for the convenience of the Examiner. As the filing date of the present application is after June 30, 2003, copies of U.S. patents are no longer required by 37 C.F.R. § 1.98(a)(2) and copies of the listed U.S. patents are not included herewith.

In accordance with 37 C.F.R §§ 1.97(g),(h), this Information Disclosure Statement is not to be construed as a representation that a search has been made, and is not to be construed to be an admission that the information cited is, or is considered to be, material to patentability as defined in 37 C.F.R. § 1.56(b).

The present Information Disclosure Statement is being filed prior to the receipt of a first Official Action reflecting an examination on the merits and hence is timely filed in accordance with 37 C.F.R. § 1.97(b). No fees are due in connection with the filing of this Information Disclosure Statement. However, should any fees under 37 C.F.R. §§ 1.16 to 1.21 be deemed necessary for any reason relating to these materials, the Assistant Commissioner is hereby authorized to deduct said fees from Williams, Morgan & Amerson, P.C., Deposit Account No. 50-0786/4100.003200.

Respectfully submitted,  
Williams, Morgan & Amerson, P.C.  
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Date: October 8, 2004

Form PTO-1449 (modified)

List of Patents and Publications for Applicant's

## INFORMATION DISCLOSURE STATEMENT

(Use several sheets if necessary)

Atty. Docket No.  
4100.003200Serial No.  
10/625,839Applicants  
George J. Brewer, Sofia D. Merajver and Dimitri  
CoucouvanisFiling Date:  
July 23, 2002Group:  
1614U.S. Patent Documents  
*See Page 1 and 2*Foreign Patent Documents  
*See Page 2*Other Art  
*See Pages 2 - 14*

## U.S. Patent Documents

Exam. Init.	Ref. Des.	Document Number	Date	Name	Class	Sub Class	Filing Date of App.
	A1	4,762,705	08/09/88	Rubin	424	85	
	A2	5,057,302	10/15/91	Johnson <i>et al.</i>	424	1.1	
	A3	5,100,885	03/31/92	Abrams <i>et al.</i>	514	184	
	A4	5,169,858	12/08/92	Rubin	514	365	
	A5	5,385,933	01/31/95	Rabinovitz <i>et al.</i>	514	499	
	A6	5,563,132	10/08/96	Bodaness	514	185	
	A7	5,697,902	12/16/97	Goldenberg	604	49	
	A8	5,565,491	10/15/96	Schieven	514	492	
	A9	5,512,559	04/30/96	Skalkos <i>et al.</i>	514	185	
	A10	5,443,816	08/22/95	Zamora <i>et al.</i>	424	1.69	
	A11	5,391,547	02/21/95	Cole <i>et al.</i>	514	184	
	A12	4,952,607	08/28/90	Sorenson <i>et al.</i>	514	589	
	A13	4,766,226	08/23/88	Hill <i>et al.</i>	556	18	
	A14	4,678,667	07/07/87	Meares <i>et al.</i>	424	85	
	A15	RE 35,458	02/18/97	Azuara	556	116	
	A16	5,112,598	05/12/92	Biesalski	424	46	
	A17	5,527,533	06/18/96	Tso <i>et al.</i>	424	422	
	A18	5,556,611	09/17/96	Biesalski	424	46	
	A19	5,583,153	12/10/96	Brahn	514	449	
	A20	5,970,974	10/26/99	van der Linden <i>et al.</i>	128	200.16	

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Form PTO-1449 (modified)		Atty. Docket No. 4100.003200	Serial No. 10/625,839
List of Patents and Publications for Applicant's  INFORMATION DISCLOSURE STATEMENT  (Use several sheets if necessary)		Applicants George J. Brewer, Sofia D. Merajver and Dimitri Coucouvani	
		Filing Date: July 23, 2002	Group: 1614
U.S. Patent Documents <i>See Page 1 and 2</i>	Foreign Patent Documents <i>See Page 2</i>	Other Art <i>See Pages 2 - 14</i>	

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	A21	5,954,047	09/21/99	Armer <i>et al.</i>	128	200.23	
	A22	5,950,619	09/14/99	van der Linden <i>et al.</i>	128	200.16	
	A23	5,698,155	12/16/97	Grosswald <i>et al.</i>	264	402	
	A24	5,639,725	06/17/97	O'Reilly <i>et al.</i>	514	12	
	A25	4,765,539	08/23/88	Noakes <i>et al.</i>	239	3	
	A26	3,916,899	11/04/75	Theeuwes <i>et al.</i>	128	260	
	A27	3,845,770	11/05/74	Theeuwes <i>et al.</i>	128	260	
	A28	4,604,278	08/05/86	Reilly <i>et al.</i>	423	517	
	A29	4,343,746	08/10/82	Anglin <i>et al.</i>	556	57	
	A30	2,909,541	10/20/59	Hugel	260	429	
	A31	6,703,050	03/09/04	Brewer <i>et al.</i>	424	641	

### Foreign Patent Documents

Exam. Init.	Ref. Des.	Document Number	Date	Country	Class	Sub Class	Translation Yes/No
	B1	EP 1 107 795 B1	Nov. 27, 2002	EP			
	B2	EP 1 234 585 A2	Aug. 28, 2002	EP			
	B3	WO 00/13712	Mar. 16, 2000	PCT			
	B4	WO 2004/009072	Jan. 29, 2004	PCT			

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### Other Art (Including Author, Title, Date, Pertinent Pages, Etc.)

Exam. Init.	Ref. Des.	Citation
	C1	Allen and Solomons, "Normal Intestinal Mechanisms in the Absorption of Copper," In: Absorption and Malabsorption of Mineral Nutrients, Solomons and Rosenberg, Eds., Alan R. Liss, Inc., New York, 12:199-229, 1984.
	C2	Alpem-Elran and Brem, "Angiogenesis in Human Brain Tumors: Inhibition by Copper Depletion," <i>Neurological Surgery</i> , pp. 498-500, publication date unknown.
	C3	Brem <i>et al.</i> , "Anticopper Treatment Inhibits Pseudopodial Protrusion and the Invasive Spread of 9L Gliosarcoma Cells in the Rat Brain," <i>Neurosurgery</i> , 26:391-396, 1990.
	C4	Brem <i>et al.</i> , "Inhibition of Angiogenesis and Tumor Growth in the Brain. Suppression of Endothelial Cell Turnover by Penicillamine and the Depletion of Copper, an Angiogenic Cofactor," <i>Am. J. Pathol.</i> , 137(5):1121-1142, 1990.
	C5	Brem <i>et al.</i> , "Tetrathiomolybdate, A Chelator of Copper, Reduces Intracerebral Peritumoral Edema in Rats," <i>Proc. Amer. Assoc. Cancer Res.</i> , 33:76, Abstract 455, 1992.
	C6	Bremner <i>et al.</i> , "Copper Metabolism in Rats Given di-or trithiomolybdates," <i>J. Inorg. Biochem.</i> , 16: 109, 1982.
	C7	Brewer and Yuzbasiyan-Gurkan, "Wilson Disease," <i>Medicine</i> , 71(3):139-164, 1992.
	C8	Brewer and Yuzbasiyan-Gurkan, "Wilson's Disease," In: Textbook of Clinical Neuropharmacology and Therapeutics, 2nd Edition, Klawans <i>et al.</i> , Eds., Raven Press, New York, pp. 191-205, 1992.
	C9	Brewer and Yuzbasiyan-Gurkan, "Wilson's Disease: An Update, with Emphasis on New Approaches to Treatment," <i>Dig. Dis.</i> , 7(4):178-193, 1989.
	C10	Brewer, "Interactions of Zinc and Molybdenum With Copper in Therapy of Wilson's Disease," <i>Nutr.</i> , 11(1 Suppl):114-116, 1995.
	C11	Brewer, "Practical Recommendations and New Therapies for Wilson's Disease," <i>Drugs</i> , 50(2):240-249, 1995.
	C12	Brewer, "Thiomolybdates in the Treatment of Wilson's Disease," <i>Arch. Neurol.</i> , 49:132-133, 1992.
	C13	Brewer, "Zinc in the Treatment of Wilson's Disease," <i>Nutrition and the MD.</i> 19(12), 1993.
	C14	Brewer <i>et al.</i> , "Treatment of Wilson's disease with Ammonium Tetrathiomolybdate. I Initial Therapy in 17 Neurologically Affected Patients," <i>Arch. Neurol.</i> , 51(6):545-554, 1994.
	C15	Brewer <i>et al.</i> , "Use of Zinc Acetate to Treat Copper Toxicosis in Dogs," <i>JAVMA</i> , 201:564-568, 1992.

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	C16	Brewer <i>et al.</i> , "Treatment of Wilson's Disease with Zinc XIII: Therapy with Zinc in Presymptomatic Patients from the Time of Diagnosis," <i>J. Lab. Clin. Med.</i> , 123:849-858, 1994.
	C17	Brewer <i>et al.</i> , "Initial therapy of Wilson's Disease Patients with Tetrathiomolybdate," <i>Arch. Neurol.</i> , 48(1):42-47, 1991.
	C18	Brewer <i>et al.</i> , "Treatment of Wilson's Disease with Zinc III. Prevention of Reaccumulation of Hepatic Copper," <i>J. Lab. Clin. Med.</i> , 109:526-531, 1987.
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	C21	Brewer <i>et al.</i> , "Treatment of Wilson's Disease with Ammonium Tetrathiomolybdate II. Initial Therapy in 33 Neurologically Affected Patients and Follow-up on Zinc Therapy," <i>Arch. Neurol.</i> , 53:1017-1025, 1996.
	C22	Brewer <i>et al.</i> , "The Use of <sup>64</sup> Copper Measurements to Diagnose Canine Copper Toxicosis," <i>J. Vet. Int. Med.</i> , 6:41-43, 1992.
	C23	Brewer <i>et al.</i> , "Worsening of Neurological Syndrome Upon Initial Treatment of Wilson's Disease Patients with Penicillamine," <i>Arch. Neurol.</i> , 44:490-493, 1987.
	C24	Brewer <i>et al.</i> , "Development of Neurologic Symptoms in a Patient with Asymptomatic Wilson's Disease Treated with Penicillamine," <i>Arch. Neurol.</i> , 51:304-305, 1994.
	C25	Brewer <i>et al.</i> , "Zinc Therapy of Wilson's Disease VIII. Dose Response Studies," <i>J. Trace Elem. Exp. Med.</i> , 3:227-234, 1990.
	C26	Brewer <i>et al.</i> , "Treatment of Wilson's Disease with Zinc: IX. Response of Serum Lipids," <i>J. Lab. Clin. Med.</i> , 118:466-470, 1991.
	C27	Brewer <i>et al.</i> , "Treatment of Wilson's Disease with Zinc XI. Interaction with Other Anticopper Agents," <i>J. Amer. Coll. Nut.</i> , 12(1):26-30, 1993.
	C28	Brewer <i>et al.</i> , "Treatment of Wilson's Disease with Zinc XII. Dose Regimen Requirements," <i>Amer. J. Med Sci.</i> , 305(4):199-202; 1993.
	C29	Brewer <i>et al.</i> , "Molecular Genetics and Zinc-Copper Interactions in Human Wilson's Disease and Canine Copper Toxicosis," In: <i>Essential and Toxic Trace Elements in Human Health and Disease: An Update</i> , Prasad, Ed., Allan R. Liss, New York, PCBR 380:129-145, 1993.

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	C30	Brewer <i>et al.</i> , "Treatment of Wilson's Disease with Zinc VI. Initial Treatment Studies," <i>J. Lab. Clin. Med.</i> , 114: 633-638, 1989.
	C31	Brewer <i>et al.</i> , "Treatment of Wilson's Disease," <i>Sem. Neural.</i> , 7:209-220, 1987.
	C32	Coucouvanis <i>et al.</i> , "An Inorganic Functional Group Approach to the Systematic Synthesis and Reactivity Studies of Binuclear Mo/S and Mo/S/O Complexes," <i>Polyhedron</i> , 8(13/14):1705-1716, 1989.
	C33	Coucouvanis <i>et al.</i> , "Dinuclear Fe-Mo-S Complexes Containing the FeS <sub>2</sub> Mo Core. Syntheses, Ground-State Electronic Structures, and Crystal and Molecular Structures of the [(C <sub>6</sub> H <sub>5</sub> ) <sub>4</sub> P] <sub>2</sub> [C <sub>6</sub> H <sub>5</sub> S] <sub>2</sub> FeS <sub>2</sub> MoS <sub>2</sub> ], [(C <sub>2</sub> H <sub>5</sub> ) <sub>4</sub> N] <sub>2</sub> [(C <sub>6</sub> H <sub>5</sub> S) <sub>2</sub> FeS <sub>2</sub> WS <sub>2</sub> ], and [(C <sub>6</sub> H <sub>5</sub> ) <sub>4</sub> P] <sub>2</sub> [(S) <sub>3</sub> FeS <sub>2</sub> MS <sub>2</sub> ] (M = Mo, W) Complexes," <i>Inorg. Chem.</i> , 22:293-308, 1983.
	C34	Coucouvanis <i>et al.</i> , "Heterodinuclear Di-μ-Sulfido Bridged Dimers Containing Iron and Molybdenum or Tungsten. Structures of (PhP) <sub>2</sub> (FeMS <sub>9</sub> ) Complexes (M = Mo, W)," <i>J. Am. Chem. Soc.</i> , 102:1730-1732, 1980.
	C35	Coucouvanis <i>et al.</i> , "Successful Isolation of a Reduced Tetrathiometalate Complex. Synthesis and Structural Characterization of the [(MoS <sub>4</sub> ) <sub>2</sub> Fe] <sup>3-</sup> Trianion," <i>J. Am. Chem. Soc.</i> , 102:6644-6646, 1980.
	C36	Coucouvanis <i>et al.</i> , "Synthesis and Structural Characterization of [(No) <sub>2</sub> FeS <sub>2</sub> MoS <sub>2</sub> ] <sup>2-</sup> A Dinitrosyl Complex Containing the FeS <sub>2</sub> MoS <sub>2</sub> Core," <i>Inorg. Chim. Acta</i> , 53:L135-L137, 1981.
	C37	Coucouvanis <i>et al.</i> , "Synthesis of Thiomolybdenyl Complexes with [Mo <sub>2</sub> (S) <sub>2</sub> (O) <sub>2</sub> ] <sup>2+</sup> Cores and Substitutionally Labile Ligands. Crystal and Molecular Structure of the [Mo <sub>2</sub> O <sub>2</sub> S <sub>4</sub> (DMF) <sub>3</sub> ] Complex," <i>Inorg. Chem.</i> , 27:3272-3273, 1988.
	C38	Coucouvanis <i>et al.</i> , "Trinuclear Fe-M-S Complexes Containing a Linear Fe-M-Fe Array and a Bridging S <sub>2</sub> MS <sub>2</sub> Unit. Electronic Structures and Crystal and Molecular Structures of the [(C <sub>6</sub> H <sub>5</sub> ) <sub>4</sub> P] <sub>2</sub> [Cl <sub>2</sub> FeS <sub>2</sub> MS <sub>2</sub> FeCl <sub>2</sub> ] (M = Mo, W) Complexes," <i>Inorg. Chem.</i> , 23:741-749, 1984.
	C39	Coucouvanis, "Fe-M-S Complexes Derived from MS <sub>4</sub> <sup>2-</sup> Anions (M = Mo, W) and Their Possible Relevance as Analogues for Structural Features in the Mo Site of Nitrogenase," <i>Acc. Chem. Res.</i> , 14:201-209, 1981.
	C40	Coucouvanis, "Syntheses, Structures, and Reactions of Binary and Tertiary Thiomolybdate Complexes Containing the (O)Mo(S <sub>x</sub> ) and (S)Mo(S <sub>x</sub> ) Functional Groups (x = 1,2,4)," <i>Adv. Inorg. Chem.</i> , 45:1-73, 1998.

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	C41	Engleka and Maciag, "Inactivation of Human Fibroblast Growth Factor-1 (FGF- 1) Activity by Interaction with Copper Ions Involves FGF-1 Dimer Formation Induced by Copper-Catalyzed Oxidation," <i>J. Biol. Chem.</i> , 267:11307-11315, 1994.
	C42	Fell <i>et al.</i> , "Gut Pathology of Rats Dosed with Tetrathiomolybdate," <i>J. Corn. Pathol.</i> , 89:495, 1979.
	C43	Folkman, "Angiogenesis," <i>The Journal of Biological Chemistry</i> , 267(16):10931-1 0934, 1992.
	C44	Folkman and Klagsbrun, "Angiogenic Factors," <i>Science</i> , 23:442-447, 1987.
	C45	Folkman, "Angiogenesis in Cancer, Vascular, Rheumatoid and Other Disease," <i>Nature Med.</i> , 1:27-31, 1995.
	C46	Folkman, "The Influence of Angiogenesis Research on Management of Patients with Breast Cancer," <i>Breast Cancer Res. Treat.</i> , 36(2):109-118, 1995.
	C47	Folkman, "Anti Angiogenic Therapy," In: <i>Cancer: Principles and Practice of Oncology</i> , Lippincott-Raven Publishers, pp. 3075-3085, 1997.
	C48	Gooneratne <i>et al.</i> , "An Investigation of the Effects of Inn Venous Administration of Thiomolybdate on Copper Metabolism in Chronic Cu-Poisoned Sheep," <i>Br. J. Nutr.</i> , 46:469, 1981.
	C49	Gooneratne <i>et al.</i> , "Intravenous Administration of Thiomolybdate for the Prevention and Treatment of Chronic Copper Poisoning in Sheep," <i>Br. J. Nutr.</i> , 46:457, 1981.
	C50	Gross <i>et al.</i> , "Inhibition of Basic Fibroblast Growth Factor-Induced Angiogenesis and Glioma Tumor Growth In Vivo in Copper Depleted Rats," <i>Proc. Amer. Assoc. Cancer Res.</i> , 32:57, Abstract 338, 1991.
	C51	Gullino, "Considerations on the Mechanism of the Angiogenic Response," <i>Anticancer Res.</i> , 6(2):153-158, 1986.
	C52	Hadjikyriacou and Coucouvanis, "New Members of the $[\text{Mo}_2(\text{S})_n(\text{S}_2)_{6-n}]^{2-}$ Series. Synthesis, Structural Characterization, and Properties of the $[\text{Mo}_2\text{S}_9]^{2-}$ , $[\text{Mo}_2\text{S}_7]^{2-}$ and $[\text{Mo}_2\text{S}_6]^{2-}$ Thioanions," <i>Inorg. Chem.</i> , 26:2400-2408, 1987.
	C53	Hill <i>et al.</i> , "Treatment of Wilson's Disease with Zinc II. Validation of Oral $^{64}\text{Cu}$ Uptake with Copper Balance," <i>Am. J. Med. Sci.</i> , 12:344, 1986.
	C54	Hill <i>et al.</i> , "Treatment of Wilson's Disease with Zinc, I: Oral Zinc Therapy Regimens," <i>Hepatology</i> , 7:522-528, 1987.

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	C55	Hourani and Demopoulos, "Inhibition of S-91 Mouse Melanoma Metastases and Growth by D-Penicillamine," <i>Laboratory Investigation</i> , 21(5):434-438, 1969.
	C56	Kanatzidis and Coucouvanis, "Structure of Bis(tetraethylammonium) Tetrathiomolybdate(VI), $2C_8H_{20}N^+MoS_4^{2-}$ ," <i>Acta Cryst.</i> , C39:835-838, 1983.
	C57	Lee <i>et al.</i> , "The Treatment of Wilson's Disease with Zinc VII. Protection of the Liver for Copper Toxicity by Zinc Induced Metallothionein in a Rat Model," <i>J. Lab. Clin. Med.</i> , 114:639-645, 1989.
	C58	Marshall <i>et al.</i> , "Phase I Trial of Orally Administered Pentosan Polysulfate in Patients with Advanced Cancer," <i>Clin. Cancer Res.</i> , 3:2347-2354, 1997.
	C59	Merajver <i>et al.</i> , "Copper Depletion as an Anti-Angiogenic Strategy in HER2-neu Transgenic Mice," Proceedings of Special AACR Conference on Angiogenesis and Cancer, Abstract #B-II, January 22-24, 1998.
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